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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/686,161

10/15/2003

R. Terry Dunlay

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EXAMINER

WHALEY, PABLO S

ART UNIT

PAPER NUMBER

1631

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

03/16/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/686,161

Applicant(s)

DUNLAY, R.

Examiner

Pablo Whaley

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely-filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10/15/2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 44-56 is/are pending in the application.
- 4a) Of the above claim(s) 51 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 44-50 and 52-56 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 08/18/2006 and 1/12/2005.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### *CLAIMS UNDER EXAMINATION*

An action on the merits of newly added claims 44-50 and 52-56 follows. Claims 1-43 have been canceled.

### *OBJECTION*

Claim 51 is objected to because of the following informalities: Claim 51 is a duplicate of claim 50. Accordingly, claim 51 is withdrawn from consideration and has not been further treated on the merits.

### *INFORMATION DISCLOSURE STATEMENT*

The information disclosure statements filed 08/18/2006 and 1/12/2005 have been considered in full.

### *DRAWINGS*

Drawings filed 10/15/2003 have been accepted.

### *PRIORITY*

Priority to US Provisional Applications 60/456,271, filed 3/19/2003 and 60/532,487, filed 12/26/2003, and 60/543,576, filed 2/11/2004 has been acknowledged.

### CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 44-50 and 52-56 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter.

The instant claims are generally directed to a machine readable storage system comprising a program containing a set of instructions (i.e. process). A statutory process must include a step of a physical transformation of matter, or produce a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999))].

It is noted that while claim 44 recites a series of procedures directed to defining cellular compartment masks, determining intensities of luminescent signals, and determining a ratio of intensity signals or a difference of intensity of signals, these procedures are not active method steps. Thus, the instant claims comprise steps that do not result in a physical transformation of matter, as the claimed method steps are not limited to physical steps (i.e. steps done by a user), and therefore encompass non-physical method steps that may be practiced inside of a computer (i.e. *in-silico*). Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. communicated to a user), and useful result (i.e. a specific and substantial). In the instant case, the claims ultimately result in determining a ratio or a difference of signals, and thus lack a tangible result as nothing is communicated to a user such that it is useful to one skilled in the

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art. Furthermore, the instructions lack a functional relationship to the machine readable storage medium, and thus are considered non-functional descriptive material. Non-functional descriptive material stored on a computer-readable medium is not statutory subject matter (e.g. music stored on a compact disk). For these reasons, the instant claims are not statutory.

This rejection could be overcome by amending the claims to recite a computer readable medium comprising a program containing instructions, wherein the program result is "displayed" or "outputted" (e.g. output to a user, a display, a memory, or another computer, etc.), or by amending the claims to include a step of a physical transformation of matter (e.g. assay). For an updated discussion of statutory considerations with regard to non-functional descriptive material and computer-related inventions, see the Guidelines for Patent Eligible Subject Matter in the MPEP 2106, Section IV.

#### **CLAIM REJECTIONS - 35 USC §112, 1<sup>st</sup> Paragraph**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 44-50 and 52-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for translocation between a cell nucleus and a cell cytoplasm, does not reasonably provide enablement for detecting translocation of a cellular component of interest between any said first and second cellular compartments on or within individual cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below which leads to the determination that the above claim lacks enablement due to undue experimentation being required to make and use the invention. In the instant case, the claimed subject matter lacks enablement for the following reasons:

The instant claims are directed to a machine readable storage medium comprising a program containing procedures comprising: (a) defining a first and second cellular compartment mask in multiple individual cells from luminescent signals obtained from a plurality of luminescent reporter molecules; (b) determining an intensity of the luminescent signals from the "at least second" reporter molecule in the first cellular compartment mask and the second cellular compartment mask; and (c) determining a ratio and/or a difference of the intensity of luminescent signals from the at least second reporter molecule in the first cellular compartment mask and the second cellular compartment mask, wherein the ratio and/or difference provides a measure of translocation of the cellular component of interest.

Computer-assisted methods for detecting the translocation of cellular components of interest between cellular compartments are well known in the art. Speicher et al. [Bioimaging, 1996, Vol. 4, p.52-64] teach steps directed to probe hybridization [p.53, Section 2.1], the detection of

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fluorescence intensity values for multiple fluorescent probes at different time periods [p 54, Section 2.3], as well as the calculation of segmentation masks for each probe [p.55, Sections 3.3 and 3.4]. Furthermore, Nederlof et al. [Cytometry, 1992, Vol. 13, p.839-845] teach methods of in situ hybridization using double-labeled probes for fluorescence ratio measurements, wherein ratios between multiple probes are determined based on fluorescent intensity values [Fig. 1 and 2]. Claim 44, step c, however, only requires a ratio of intensity signals from the "at least second" luminescent reporter. Thus, the teachings the prior art are not consonant with the instant claims.

Furthermore, regarding claim 44, step (a), the specification discloses "masks" as a term of art, wherein masks are binary images obtained as the output of segmentation and thresholding procedures [p.32, ¶ 3 and p.40, ¶ 2]. These limitations are not consonant with the instant claims. The specification also discloses methods for obtaining "cytoplasmic masks" based on average fluorescence intensities [p.33, ¶ 2 and p.34, ¶ 1]. Again, the instant claims do not recite any such limitations. Therefore one of skill in the art would have to guess as to the intended method for defining cellular masks. Claim 44, step a, also provides a first reporter molecule "to identify the individual cells" and a second reporter molecule "to report on a cellular component of interest." In both cases, it is unclear how cells are "identified" by said first reporter molecule, and how a cellular component of interest is "reported on" by a second reporter molecule [Wands factors (2), (4), (8)].

Furthermore, regarding the procedure of claim 44, steps (a)-(c), there is no step directed to "detecting the translocation of a cellular component" [See 112 2<sup>nd</sup> below]. Therefore, it is unclear how determining a ratio and/or a difference of the intensity of luminescent signals from the at least second reporter molecule in the first cellular compartment mask and the second cellular compartment mask results in detecting the translocation of a cellular component of interest. The

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specification discloses an automated method for screening the distribution of a transcription factor by labeling the nuclei with a DNA specific fluorophore, calculating average antibody fluorescence in nuclear and cytoplasmic mask regions, and calculation of the "NucCyt Difference" [p.46 and 47]. The instant claims do not recite any such limitations. Furthermore, while the said "NucCyt Difference" was found to strongly correlate with inhibition of translocation [p.48, ¶ 2] this is not specific support for "detecting the translocation of a cellular component of interest." Furthermore, instant claim 55 recites the limitation "the procedures are used to test an effect of a test compound on translocation of the cellular component of interest." However, it is unclear how the procedures of claim 44 are "used to test an effect" of a test compound, as no correlation between the result of claim 44 directed to ratios and/or differences of intensities and "effects of test compound" have are recited in the instant claims. Therefore one of skill in the art would have to guess as to the type of effect that is intended by applicant. The specification discloses methods screening for compounds that inhibit or induce hypertrophy in myocytes [p.49, Example 2]. However, the instant claims do not recite such limitations. [Wands factors (2), (4), (8)]. Furthermore, claim 56 recites "steps (a) through (c) are performed at multiple time periods", which appears to indicate the claimed procedure may be directed to kinetic analysis of cellular events. The specification also discloses the sequential time-based acquisition of cellular images [Fig. 10] and [Fig. 14], and scanning after different time periods [p.43, ¶ 1]. However these limitation are not consonant with the instant claims, as the instant claims do not provide any steps for "comparing" intensity values acquired from reporter molecules at different time points. Therefore, one of skill in the art would have to guess as to which type of luminescent reporter molecules should be used (i.e. fluorescent dyes, fluorescent labeled antibodies, etc.), and whether the procedure for detecting the translocation of said cellular component is based



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on ratio and/or intensity translocation, time-sequence tracking of spots intensity data and subsequent intensity comparison, or on some other kinetic measure.

Despite the high level of skill in the art, as the steps of the instant claims are not limited to translocation between a cell nuclei and cytoplasm and lack sufficient guidance as to the imaging methods for defining cellular compartments, the types of luminescent reporter molecules used, and the method detecting the translocation of cellular components of interest, as set forth above, it would require undue experimentation by one of skill in the art to predictably practice the instantly claimed invention. [Wands factors (1), (2), (6), (7)].

#### **CLAIM REJECTIONS - 35 USC § 112, 2<sup>nd</sup> Paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-50 and 52-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 recites "detecting the translocation of a cellular component of interest between a first cellular compartment and a second cellular compartment on or within individual cells on an array of locations which contain multiple cells" in the preamble. However, the steps of the instant claim do not specifically require a "cellular component of interest", nor do they result in the "detection" of the translocation of said cellular component of interest. Therefore it is unclear in what way the instant claim achieves the purpose of the preamble. Clarification is requested. The Examiner has broadly interpreted this claim for purposes of applying prior art.

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Claim 44, step a, recites the step of “defining a first cellular compartment mask and a second cellular compartment mask...obtained from a plurality of luminescent reporter molecules.” Claim 44, step a, then further limits said reporter molecules “to identify” individual cells and “to report on” cellular components of interest. Therefore, it is unclear whether said reporter molecules serve to define “cellular compartment masks”, or to identify cells and report on cellular components of interest, or both. If the later, it is unclear in what way said reporter molecules relates to cellular compartment masks, identifying cells, and reporting on cellular components of interest. Clarification is requested. The Examiner has broadly interpreted this claim for purposes of applying prior art.

Claim 44, step a, recites a “reporter molecule to identify the individual cells.” It is unclear is this limitation is intended to be an active method step (i.e. identifying), an intended use of said reporter molecule, or otherwise. Clarification is requested. The Examiner has broadly interpreted this limitation for purposes of applying prior art.

Claim 44, step a, recites a “reporter molecule to report on a cellular component of interest.” It is unclear is this limitation is intended to be an active method step (i.e. reporting), an intended use of said reporter molecule, or otherwise. Clarification is requested. The Examiner has broadly interpreted this limitation for purposes of applying prior art. Claims 45-56 are rejected as they depend from rejected claim 44.

**CLAIM REJECTIONS - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 45-49, 53, and 56 are rejected under 35 U.S.C. 102 (b) as being anticipated by Kamentsky et al. (US 5,427,910; Issued Jun. 27, 1995).

Kamentsky et al. teach a method of fluorescent cytogenetic analysis that provides for the optical detection of chromosomal abnormalities (i.e. translocations). Kamentsky et al. teach the following aspects of the instant claims:

- Digital scanning methods for defining first and second cellular regions based on optical signals obtained from fluorescent labels for multiple individual cells [Fig. 6], [Col. 7, lines 15-30], and [Col. 12, lines 15-60], as in claim 44, step a.
- Determining intensity signals from a plurality of fluorescent spots from each cellular region [Col. 13, lines 12-25], as in claim 44, step b.
- Measuring translocation based on a 'distance' parameter that incorporates fluorescent intensity information from two different dyes [Col. 15, lines 10-37], which is a teaching for a difference in intensity as in claim 44, step c.

Kamentsky also teach the following aspects of dependent claims 45-49, 53, and 56: programs and software (i.e. machine readable storage medium) [Col. 12, 1-20] and computer system

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comprising memory (i.e. database) [Col. 8, lines 1-20] for implementing the above procedures; listing of property values for each region [Col. 13, lines 45-50] and reading of data files (i.e. summary data) for user review [Col. 16, lines 5-15]; lives cells and performing image scanning at different times [Col. 13, lines 50-60] and [Ref. Claim 22].

### **Obviousness-Type Double Patenting Rejection**

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R. 1.321 (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. 3.73(b).

Claims 44, 50, 51, 52, 53, 55, and 56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, and 8 of US 6,671,624, issued Dec. 30, 2003. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the broadly encompassing scope of

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the instantly claimed invention causing the inventions to have overlapping embodiments. The instant claims and those of US 6,671,624 recite the same method steps, with minor variations. For example, claim 44 of the instant application, directed to program comprising a procedure for detecting the translocation of a cellular component on interest between a first and second cellular compartment, recites a first reporter molecule to identify the individual cells, and a second reporter molecule to report on a cellular component of interest. Claim 1, steps b and e, of US 6,671,624, while directed to a program comprising a procedure for detecting the distribution of macromolecules of interest, recites "identifying" cells from fluorescent reporter molecules and calculation of ratios for reporter molecules that report on macromolecules of interest. It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to use fluorescent signals of reporter molecules for identification of individual cells and for reporting on cellular components of interest for detecting the translocation of a cellular component of interest, as distribution is inherently a form of translocation. This is a obviousness-type double patenting rejection because the conflicting claims have in fact been patented.

## CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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